

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : James A. Laugharn, Jr., *et al.* Art Unit : 1744
Serial No. : 10/770,241 Examiner : Elizabeth L. McKane
Filed : February 2, 2004 Conf. No. : 9463
Title : RAPID CRYOBARIC STERILIZATION AND VACCINE PREPARATION

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8

The undersigned hereby certifies that this document is being electronically filed in accordance with 37 C.F.R. § 1.6(a)(4), on the 12th day of January 2009.

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Commissioner for Patents
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APPELANT'S REVISED BRIEF ON APPEAL PURSUANT TO 37 C.F.R. § 41.37

Dear Sir:

This Appeal Brief is filed in response to the Notification of Non-Compliant Appeal Brief dated December 12, 2008 and in response to the final Office Action dated September 27, 2005. The fee under 37 C.F.R. § 41.20(2)(2) was previously paid. If any fee is deficient or if there are any further fees due, including any extension fees, please charge Deposit Account No. 50/2762.

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I. Real Party in Interest (37 C.F.R. § 41.37(c)(i))

Pressure Biosciences, Inc. is the Real Party in Interest and was formerly known as Boston Biomedica, Inc. including its wholly owned subsidiary BBI Bioseq, Inc.

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II. Related Appeals and Interferences (37 C.F.R. § 41.37(c)(ii))

There are no prior or pending appeals, interferences, or judicial proceedings related to the present application.

III. Status of Claims (37 C.F.R. § 41.37(c)(iii))

Claims 1-31 were originally filed. Claims 32-37 were added in a Response filed July 5, 2005. Claims 3-5, 8, and 15-31 were previously cancelled.

Without adding new subject matter, claims 7, 32, 33, 36, and 37 are currently amended to correct typographical errors. Amendments are shown by strikethrough for deleted matter and underlining for added matter.

Claims 1, 2, 6, 7, 9-14, and 32-37 are pending with claim 1 being the only pending independent claim.

All of the pending claims were rejected under 35 U.S.C. § 103(a) as would have been obvious over the disclosure of Hashizume *et al.*, in “Kinetic Analysis of Yeast Inactivation by High Pressure Treatment at Low Temperatures” (hereinafter “Hashizume”) in view of the disclosure of Hayakawa *et al.*, in “Oscillatory Compared with Continuous High Pressure Sterilization on *Bacillus stearothermophilus* Spores” (hereinafter “Hayakawa”).

Claims 7 and 36 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants have submitted claim amendments, which have not yet been entered, addressing this rejection.

Claims 32 and 33 are objected to due to a misspelling of the word “macromolecule.” This typographical error has been corrected in the amendment filed but not yet entered.

Applicants appeal the rejection of claims 1, 2, 6, 7, 9-14, and 32-37 and request entry of the amendments to overcome the objections.

A copy of the claims as pending is attached as a Claims Appendix, beginning on page 12.

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IV. Status of Amendments (37 C.F.R. § 41.37(c)(iv))

Editorial amendments to claims 7, 32, 33, and 36 were submitted on October 23, 2006, but were not entered by the Examiner because Applicants made errors in that amendment. The appendix of claims attached hereto contains the correct listing of the claims as they existed before the amendment of October 23, 2006. On January 10, 2008, Applicants submitted an amendment correctly showing changes to the pre-October 23, 2006 claims and making the editorial amendments sought to be made on that date.

Thus, claims 7, 32, 33, 36, and 37 are currently amended to correct typographical errors without adding new subject matter. Amendments to these dependent claims are shown by strikethrough for deleted matter and underlining for added matter.

V. Summary of Claimed Subject Matter (37 C.F.R. § 41.37(c)(v))

The claims recite methods of sterilizing a material. (See e.g., Specification at page 3, lines 23-26.) The methods include providing the material at an initial pressure, and while maintaining the material in a temperature range below 45 °C, (See e.g., Specification at page 3, line 23 to page 4, line 1.) increasing the pressure to an elevated pressure, and then decreasing the pressure below the elevated pressure and cycling the pressure between a decreased pressure and the elevated pressure at least two times to provide a sterilized material. (See e.g., Specification at page 5, lines 1-5.)

Independent claim 1 is directed to a method for sterilizing a material. (see, for example, Specification at page 3, lines 23-26.) The method typically comprises providing said material at an initial pressure; and while maintaining said material in a temperature range that is below 45°C (see, for example, Specification at page 3, lines 26-31, at page 6, lines 4-29, and the Examples), increasing the pressure to an elevated pressure (see, for example, Specification at page 4, lines 23-26, at page 6, line 13 to page 7, line 12, at page 11, lines 24-30, at page 15, lines 22-28, at page 16, lines 7-19, at page 25, lines 15 *et seq.*, and the Examples), then decreasing the pressure below the elevated pressure (see, for example, Specification at page 3, lines 25-27, at page 5, lines 1-12, at page 7, lines 10-11, at page 8, line 30 to page 9, line 3, at page 10, lines 1-2 and lines 18-19, and at Examples), and cycling the pressure between a decreased pressure and the elevated pressure at least two times, thereby providing a sterilized material (see, for example, Specification at page 7, lines 19 *et seq.*, at page 10, lines 20-24, at page 12, lines 10 *et seq.*, at page 13, lines 19 *et seq.*, at page 16, lines 26 *et seq.*, and at Examples).

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VI. Grounds of Rejection to be Reviewed on Appeal (37 C.F.R. § 41.37(c)(vi))

A. Whether claims 1, 2, 6, 7, 9-14, and 32-37 would have been obvious over the disclosure of Hashizume in view of the disclosure of Hayakawa under 35 U.S.C. § 103(a).

B. Whether claims 7 and 36 are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention under the second paragraph of 35 U.S.C. § 112.

C. Whether claims 32 and 33 should be objected to due to a misspelling of the word “macromolecule.”

VII. Argument (37 C.F.R. § 41.37(c)(vii))

- A. Claims 1, 2, 6, 7, 9-14, and 32-37 would not have been obvious over the disclosure of Hashizume in view of the disclosure of Hayakawa

The pending claims recite methods of sterilizing a material by subjecting the material to cycled pressure (i.e., cycling between elevated pressure and decreased pressure) and maintaining the temperature of the material below 45 °C.

Hashizume discloses methods of inactivating *Saccharomyces cerevisiae* (a strain of yeast), using high pressure treatment. Hashizume says that “rapid inactivation took place when the temperature was above 45 °C or below -10 °C.” (See Hashizume page 1456, lines 17-19, left column.) Hashizume does not teach or suggest cycling pressure between an increased and decreased pressure, nor is Hashizume relied upon for such a teaching.

Hayakawa discloses examples of the use of oscillatory pressurization (i.e., pressure cycling) to reduce the count of thermophilic spores of *Bacillus stearothermophilus*. Hayakawa tested the effects of oscillatory pressurization on spores, demonstrating that “(o)scillatory pressurization at 70 °C completely burst each spore along the length of the spore shape.” (See Hayakawa, p. 165 and 166, RESULTS, Oscillatory pressurization, and Figure 5.)

When applying 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

(A) the claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) Reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

Applicants have limited the claimed invention to methods of sterilizing material at temperatures below 45 °C using cycled pressure. The references, when considered as a whole, do not fairly teach Applicants claimed methods. The Examiner cites Hayakawa as the only

example of using cycled pressure, and yet the temperatures used in Hayakawa fall outside Applicants' claimed ranges. Moreover, as demonstrated in Figure 3 of Hayakawa, increasing the temperature from 60 °C to 70 °C with oscillatory pressure led to a greater reduction in survivors at two different pressures (i.e., 400 MPa and 600 MPa).

Without the benefit of impermissible hindsight afforded by Applicants' claimed invention, one would not arrive at methods for sterilizing material at temperatures below 45 °C using cycled pressure. Instead, one would be motivated to use the methods clearly taught by Hayakawa. While the Examiner asserts that one would be motivated to modify the teachings of Hashizume with Hayakawa to arrive at the claimed invention, the references, when taken as a whole, more fairly suggest methods of oscillatory pressure at elevated temperatures, i.e., temperatures greater than 45 °C, such as 60 °C or 70 °C. Moreover, nothing in the combined references would provide an expectation of success when practicing the claimed invention. Rather, Hashizume notes that "No or little inactivation was observed for the pressurization below 180 MPa at temperatures between 0 °C and 40 °C." (See Hashizume page 1456, lines 17-19, left column.)

B. Claims 7 and 36 are not indefinite under 35 U.S.C. 112, second paragraph

Applicants have submitted claim amendments, which have not yet been entered, addressing these rejections. These rejections will be moot upon entry of these amendments.

C. Claims 32 and 33 should not be objected to due to a misspelling of the word "macromolecule"

Applicants have submitted claim amendments, which have not yet been entered, addressing these objections. These objections will be moot upon entry of these amendments.

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D. Conclusion

For the reasons provided herein, the rejections are improper and should be reversed. Applicants therefore request that the rejections be withdrawn and issuance of a Notice of Allowance.

VIII. Claims Appendix (37 C.F.R. § 41.37(c)(vii))

1. (Previously presented) A method for sterilizing a material, the method comprising:
providing said material at an initial pressure; and
while maintaining said material in a temperature range that is below 45°C, increasing the pressure to an elevated pressure, then decreasing the pressure below the elevated pressure, and cycling the pressure between a decreased pressure and the elevated pressure at least two times, thereby providing a sterilized material.
2. (Original) The method of claim 1, wherein the material is provided at an initial pressure of about 1 atm.
- 3-5. (Canceled)
6. (Original) The method of claim 1, wherein the elevated pressure is in the range of about 5,000 psi to about 120,000 psi.
7. (Currently amended) The method of claim 1, wherein the material comprises a desired biomolecule ~~is~~ selected from the group consisting of nucleic acids, proteins, lipids, carbohydrates, drugs, steroids, and nutrients.
8. (Canceled)
9. (Previously presented) The method of claim 1, wherein the pressure is cycled at least ten times.
10. (Previously presented) The method of claim 1, wherein the decreased pressure is half of the elevated pressure or less.

11. (Original) The method of claim 1, further comprising warming or cooling the material prior to the pressure-increasing step.

12. (Original) The method of claim 1, further comprising warming or cooling the material after the pressure-increasing step.

13. (Original) The method of claim 1, wherein the material being sterilized is selected from the group consisting of a biological sample; blood plasma, serum, or other plant, animal, or human tissue; feces; urine; sputum; medical or military equipment; a foodstuff; a pharmaceutical preparation; ascites; and a vaccine.

14. (Previously presented) The method of claim 1, wherein the material being sterilized is initially contaminated with at least one of a prion, a virus, a fungus, a protist, a nucleic acid, and a protein.

15-31. (Canceled)

32. (Currently amended) The method of claim 1 in which the sterilized material comprises a desired ~~mareromolecule~~ macromolecule.

33. (Currently amended) The method of claim 14 in which the sterilized material comprises a desired ~~mareromolecule~~ macromolecule.

34. (Previously presented) The method of claim 32 in which the desired macromolecule has a biological activity that is maintained in the sterilized material produced by the method.

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35. (Previously presented) The method of claim 32 in which the macromolecule is a protein.

36. (Currently amended) The method of claim 32 in which the sterilized material comprises an infectious agent, which is a virus.

37. (Currently amended) The method of claim 1, wherein the elevated pressure is in ~~the~~ a range of about 2,000 psi to about 120,000 psi.

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IX. Evidence Appendix (37 C.F.R. § 41.37(c)(xi))

None.

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X. Related Proceedings Appendix

None.

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XI. Conclusion

For the reasons provided, Appellant respectfully requests reversal of the rejections and issuance of a Notice of Allowance.

The brief fee was submitted with the earlier filed Appeal Brief. Please apply any other charges or credits to deposit account no. 50/2762 (reference P2028-702920).

Respectfully submitted,
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